d.) Remarks.

Applicant has amended claims 16, 19, 20, 44-46 and 49. Support for these amendments can be found in the original claims and throughout the specification (e.g. see page 3, line 26 "EA1 antigen"; and line 26 "isolated"; and page 14, line 1 "binds"). No new matter is added or new issues presented. Accordingly, claims 16-20 and 44-49 are presently pending.

Remarks Regarding 35 U.S.C. § 112, Second Paragraph

Claims 16-20 and 44-49 stand rejected, under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Applicant respectfully traverses this rejection.

The Examiner alleges that claims 16-20 and 44-49 are vague and indefinite because they do not clarify that the antibody is "isolated" and/or "purified". The Examiner further adds that it is unclear how unpurified or unisolated antibodies would be effective in a detection assay.

While not acquiescing to the Examiner's argument, Applicant has amended the relevant claims to read "isolated" antibody to expedite prosecution of this application. Applicant respectfully disagrees with the Examiner on her characterization that unpurified or unisolated antibodies would be ineffective in a detection assay. In contrast to the Examiner's suggestion, Applicant contends that, for example, serum from an animal exposed to *B. anthracis* or *B. thuringiensis* can be used in the detection method without isolation or purification. Thus, there is no need for purified or isolated antibody to allow detection using the method of the invention.

Furthermore, the Examiner alleges that claims 16-20 and 44-49 are vague and indefinite because it is unclear what is meant by the phrase "specifically reactive". Again, while not acquiescing to the Examiner's argument, Applicant has amended the relevant claims to read "specifically binds" to expedite prosecution of this application. Applicant contends that one of skill in the art would recognize that an antibody's specific reactivity is to bind an antigen.

The Examiner alleges that claims 16-20 and 44-49 are vague and indefinite because the claim does not provide structural properties that would allow one to identify the antibodies recited in the claims without ambiguity.

Applicant respectfully contends that the Examiner is confusing the requirements for adequate written description as specified in 35 U.S.C. § 112, first paragraph, with the requirements for claim definiteness as specified in 35 U.S.C § 112, second paragraph. To comply with the definiteness requirement, the claim must be definite enough to allow one of skill in the art to be appraised of what constitutes infringement. As the claims are written, one of skill in the art clearly understands the metes and bounds of the claims. Nothing more is required to satisfy the definiteness requirement.

Applicant also respectfully points out that the Examiner has mischaracterized what Applicant regards as the invention. The Examiner suggests that Applicant's invention is confined to antibodies that bind *B. anthracis*, but not *B. thuringiensis*. The specification clearly indicates that antibodies that react with *B. thuringiensis,* but not *B. anthracis* are also embodiments of this invention.

Structural properties are not required to satisfy the definiteness requirement. However, in an attempt to understand the Examiner's concern, the claims have been amended to recite an antibody that binds to EA1 antigen. The structure of the EA1 antigen is disclosed in the specification and known in the art.

Applicant respectfully requests that this rejection be withdrawn.

Remarks Regarding 35 U.S.C. § 112, First Paragraph – Enablement

Claims 16-20 and 44-49 stand rejected, under 35 U.S.C. § 112, first paragraph, as allegedly not enabled. Applicant respectfully traverses this rejection.

The Examiner states that the specification is enabling for "a diagnostic kit comprising an isolated antibody which specifically binds to an epitope of the EA1 polypeptide...." (Office Action, page 7, first paragraph). The claims have been amended to recite that the antibodies bind to EA1 and, thus, this rejection is moot.

Additionally, the Examiner alleges that the specification is non-enabling for antibodies that specifically react with *B. thuringiensis*, but not *B. anthracis* because "[i]t would take undue experimentation for one of skill in the art to identify a completely new unique antibody which

displays no cross-reactivity to other members of its Genus." (Office Action, page 7, first paragraph). Furthermore, the Examiner alleges that there is a great deal of unpredictability in finding antibodies which can distinguish between different species of *Bacillis*, and that there is very little guidance in the specification for finding an antibody unique to *B. thuringiensis*.

Applicant respectfully disagrees. Firstly, applicant respectfully notes that the Examiner provides no comments whatsoever on the methods used by applicant to produce species-specific antibodies. No steps are identified as lacking or unclear or that would not lead to applicant's expected result – species specific antibodies. Thus there is every reason to consider that a substitution of *B. thuringiensis* for *B. anthracis* would lead to the invention as claimed by applicant. Accordingly, this aspect of the rejection is no more than a mere conclusion, which, pursuant to MPEP 707.03, is to be avoided. Rejections must be well reasoned and based on available technical information. No such technical reasoning is presented, in spite of the wealth of information available on antibody production in the specification and the cited references.

Nevertheless, applicant disagrees that the discussion of how to make antibodies to species of *Bacillis* other than *B. anthracis* is brief and unenabling. The specification on pages 6-7 provides significant and specific guidance, as well as a discussion of how one of ordinary skill in the art creates antibodies to a specific species of *Bacillis*.

> *Another embodiment of the invention is directed to a method of producing a species-specific monoclonal antibody to one species of Bacillis. This method preferably comprises first immunizing a host animal with a preparation of the species of interest such as, for example B. anthracis, B. cereus or B. thuringiensis, which are all antigenically similar. . . . Preferably about seven days prior to fusion, administering an intravenous boost using a preparation from another species of the same genus as the species used during the immunization. Preferably, this species is of an antigenically similar, but not identical, species. For example, when selecting for antibodies to B. cereus, either B. anthracis or B. thuringiensis may be used as the antigenically similar source. When selecting for antibodies specific to B. anthracis, either B. cereus or B. thuringiensis may be used as the antigentically similar source. This stimulates clones that share specificity between the species of interest and the near neighbor species. However, by the time of fusion about seven days later, these clones will have diminished*

> *capacity to be fused. Next, and preferably about three days prior to fusion, administering another boost via, for example, an intravenous route (intra peritoneal, subcutaneous, etc.), with a preparation of the species of interest. This stimulates clones that haven't already been stimulated by the antigenically similar boost, the specific clones. These species-specific clones should be maximally susceptible to being fused three days later. Thus, the number of cross-reacting clones should be greatly reduced or eliminated in the fusion products and a species-specific monoclonal antibody should be favored. Additional boosts may be performed and at various times to maximize generation of anthrax-specific hybridomas, as may be determined by one of ordinary skill in the art.*" See Specification, page 6, line 14 – page 7, line 9.

One of skill in the art would know how to apply the detailed protocols for making *B. anthracis* specific antibodies in the Examples on page 10 to develop antibodies to other species of *Bacillis*, such as *B. thuringiensis*. After performing such a procedure, it would require no more than routine screening as set forth in the specification to identify species specific antibodies. The screening of monoclonal antibodies has been held to not involve an undue amount of experimentation. See In re Wands.

Furthermore, one of skill in the art would believe that there was a high expectation of success, given the ability to generate *B. anthracis*-specific antibodies as described in the pending application, and also because other references, such as the Kearney reference cited by the Examiner, show the ability to generate monoclonal antibodies to species such as *B. subtilis*.

For at least the foregoing reasons applicant contends that the disclosure is enabling and respectfully request that this ground for rejection be withdrawal.

Remarks Regarding 35 U.S.C. § 112, First Paragraph – Written Description

Claims 16-20 and 44-49 stand rejected, under 35 U.S.C. § 112, first paragraph, as allegedly not complying with the written description requirement. Applicant respectfully traverses this rejection.

The Examiner concedes that the applicant has enabled antibodies that specifically bind to the EA1 protein and suggests that the detailed structure of the antibodies is required to meet the

written description requirement. The Examiner further asserts that "[a]dequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of making or isolating it. The antibody itself is required." Applicant respectfully disagrees that the antibody is required to meet the written description requirement. The USPTO guidelines on written description describe an example of adequate written description of an antibody that has not been reduced to practice but for which a purified antigen is available.

Accordingly, Applicant respectfully contends that adequate written description is found in the currently amended claim which reads, in part, "an isolated antibody that binds EA1 antigen". The claim as amended provides sufficient structural information to meet the written description requirement as set forth by the USPTO guidelines for adequate written description of antibody claims and as set forth in the rationale for the Examiner's rejection.

Furthermore, Applicant respectfully contends that adequate written description is found in the specification for antibodies that bind *B. thuringiensis*, but not *B. anthracis*. Adequate written description requires that an applicant demonstrate possession of the invention in the disclosure of the specification. As discussed above in the section on enablement, Applicant has provided a detailed and extensive discussion and protocol on how to make *Bacillis* species-specific antibodies (specification on pages 6-7 and in the Examples on page 10). One of ordinary skill in the art would recognize from reading the disclosure that the Applicant has possession of *Bacillis* species-specific antibodies, given the detailed and unique protocol presented in the specification and the ability to generate *B. anthracis* specific antibodies as disclosed in the instant application. Moreover, possession would also be suggested to one of ordinary skill by other references, such as the Kearney reference, which was cited by the Examiner, showing the generation of monoclonal antibodies to *Bacillis* species such as *B. subtilis*.

For the foregoing reasons, Applicant contends that there is adequate written description for the pending claims and respectfully request that this ground for rejection be withdrawn.

Remarks Regarding 35 U.S.C. § 102/103

Long et al. ("Long")

Claims 16-19 and 44 stand rejected, under 35 U.S.C. § 102(a), as allegedly anticipated by or, in the alternative, under 35 U.S.C. § 103(a), as allegedly obvious over Long. Applicant respectfully traverses this rejection.

As a preliminary matter, the Examiner mischaracterizes the teachings of Long by stating that "although the reference does not specifically recite that the assay is not reactive against spores of *B. thuringiensis*, it does recite that the assay is specific for the detection and identification of *B. anthracis*. This is a mischaracterization of Long because no where in this reference do the authors state that the assay is specific for *B. anthracis*. Long merely states that "[w]e have developed antigen capture dipstick type assays for a series of infectious agents including an assay for *B. anthracis* protective antigen and one for *B. anthracis* spores. As the Examiner has already conceded, there is no teaching in Long regarding the binding of antibodies to *B. thuringiensis*. But, the Examiner alleges that because Long discloses antibodies that react with protective antigen of *B. anthracis*, these antibodies would have the inherent property of not reacting with *B. thuringiensis*, since *B. thuringiensis* does not express protective antigen. Applicant respectfully contends that this inherency argument is not valid. Just because an antibody binds protective antigen of *B.anthracis* does not mean that the antibody might not be cross-reactive with proteins found on *B. thuringiensis*. Long does not state that the antibodies bind to protective antigen and nothing else. For inherency to apply, one of skill in the art must recognize that the missing descriptive matter is necessarily present in the reference. Because of the possibility that the antibodies to protective antigen or *B. anthracis* spores described in Long may cross react to proteins found on *B. thuringiensis*, it is not necessarily true that the antibodies in Long will inherently not bind to *B. thuringiensis*.

Furthermore, Long does not enable the claimed invention. Long provides no teachings of the antibody or how to make antibodies disclosed in the abstract. In fact, according to the Examiner's own statements in the instant Office Action:

> *"The specification does not teach any other antibodies, but merely recites prophetic methods for developing antibodies specific to*

> *Bacillus species. Antibodies to species of Bacillus other than B. anthracis are described briefly on pages 6-7, yet no disclosure beyond the mere mention of the possibility of making such antibodies is provided. It would take undue experimentation for one of skill in the art to identify a completely new unique antibody which displays no cross-reactivity to other members of its Genus."* (Office Action, page 7, first paragraph).
>
> *"Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention."* (Office Action, page 7, second paragraph).

Long describes no antibody binding specificities, discloses no methods for developing antibodies or developing specific antibodies, and no antibodies that do not cross-react with other members of the same Genus. In fact, Long provides no reasonable detail at all and, thus, one of ordinary skill in the art would be unable to understand and/or carry out the invention. At least because the Examiner considers such aspects as required for enablement, and all are absent from Long, Long cannot be considered to anticipate or suggest the claimed invention.

Because Long does not teach each and every element of the claimed invention, applicant respectfully requests withdrawal of this ground for rejection.

Mesnage et al. ("Mesnage")

Claim 16 and 44 stand rejected, under 35 U.S.C. § 102(b), as allegedly anticipated by or, in the alternative, under 35 U.S.C. § 103(a), as allegedly obvious over Mesnage. The Examiner alleges that Mesnage teaches antibodies to *B. anthracis* EA1 protein. The Examiner goes on to allege that "although the reference does not specifically recite that the antibody to *B. anthracis* does not specifically react with *B. thuringiensis*, it inherently would not since the antigen to which it binds is specific to *B. anthracis* . . . The antibodies to the EA1 protein would be identical to the Applicant's antibody to the EA1 antibody, i.e., the antibodies are raised against the same antigen.." Thus, the Examiner is ascribing an inherent property to the antibodies taught

in Mesnage, namely the lack of binding to *B. thuringiensis*. Applicant respectfully contends that this inherency argument is flawed. Firstly, just because the Applicant's antibody and the antibodies in Mesnage recognize the same antigen, EA1, does not mean they have the same properties. Different properties can arise due to factors such as the antibodies recognizing different epitopes on an antigen, having different affinities, avidities, and cross reactivities, among other characteristics that could differ. Thus, the Examiner's contention that these antibodies would be identical is not necessarily true, and likely not to be the case. Finally, because of potential differences in cross-reactivity, it is not necessarily true that the antibodies described in Mesnage would not also bind to *B. thuringiensis*; the reference is silent on this point. For inherency to apply, one of skill in the art must recognize that the missing descriptive matter is necessarily present in the reference. Because of the possibility of cross reactivity of the antibodies to EA1 taught in the Mesnage reference to proteins found on *B. thuringiensis*, it is not necessarily true that these antibodies will not bind *B. thuringiensis*.

Thus, because Mesnage does not teach each and every element of the claimed invention, applicant respectfully requests withdrawal of this rejection.

Phillips et al. ("Phillips")

Claim 16 and 44 stand rejected, under 35 U.S.C. § 102(b), as allegedly anticipated by or, in the alternative, under 35 U.S.C. § 103(a), as allegedly obvious over Phillips.

The Examiner contends that Phillips teaches monoclonal antibodies against spore antigens of *Bacillis anthracis*. Furthermore, the Examiner states, "although the reference does not specifically recite that the antibody to *B. anthracis* does not specifically react with *B. thuringiensis*, it inherently would not since the antigen to which it binds is specific to *B. anthracis*". The arguments regarding the flaw in the Examiner's inherency argument from above apply as well here. Furthermore, the currently amended claims, using as an example claim 16, read "an isolated antibody that binds EA1 antigen and specifically binds spores or vegetative cells of *B. anthracis*, but not *B. thuringiensis*". Thus, Phillips does not teach or suggest each and

every element of the claimed invention. For at least this reason, applicant respectfully requests withdrawal of this rejection.

Wright et al. ("Wright")

Claims 16, 19 and 44 stand rejected, under 35 U.S.C. § 102(b), as allegedly anticipated by or, in the alternative, under 35 U.S.C. § 103(a), as allegedly obvious over Wright.

The Examiner characterizes Wright as teaching monoclonal antibodies against antigens of *Bacillis*, including *B. cereus* and *B. anthracis*. Furthermore, the Examiner states, "although the reference does not specifically recite that the antibody to *B. anthracis* does not specifically react with *B. thuringiensis* and vice versa, they inherently would not since the antigen to which the antibodies bind are specific to the particular species of *Bacillus*. Again, the arguments regarding the flaw in the Examiner's inherency argument from above apply as well here. The currently amended claims, using as an example claim 16, read "an isolated antibody that binds EA1 antigen and specifically binds spores or vegetative cells of *B. anthracis*, but not *B. thuringiensis*". Thus, Wright does not teach each and every element of the claimed invention. Thus, this reference does not satisfy the requirements for a rejection based on anticipation or obviousness under 35 U.S.C. § 102(b) or § 103(a). For at least these reasons, applicant respectfully requests withdrawal of this rejection.

Remarks Regarding 35 U.S.C. § 103

Claims 16-20 and 44-49 stand rejected, under 35 U.S.C. § 103(a), as allegedly obvious over Kearney et al. ("Kearney") in view of Loomis et al. ("Loomis").

The Examiner alleges that "Kearney teaches monoclonal antibodies that are specifically reactive to spores from different species of *Bacillis*. Furthermore, the Examiner contends that "Figure 6 shows that anti-*Bacillis* anthracis antibody specifically binds *B. anthracis* spores. Example 13, page 18, teaches a monoclonal antibody which specifically reacts with *B. anthracis*, but is not at all reactive with *B. subtilis* or *B. thuringiensis*." The Examiner has combined the

Kearney reference with the Loomis reference which teaches colloidal gold particle immunoassays.

The claimed invention, using as an example claim 16, reads "an isolated antibody that binds EA1 antigen and specifically binds spores or vegetative cells of *B. anthracis*, but not *B. thuringiensis*". Without conceding the Examiner's characterization of these references, Applicant respectfully submits that Kearney, as explained above, does not teach each and every element of the claimed invention. These missing elements are not supplied by the Loomis et al. reference. Thus, the requirements for a rejection based on obviousness, under 35 U.S.C. § 103(a), have not been met by these references. For this reason, applicant respectfully requests withdrawal of this ground for rejection.

Claims 16-19 stand rejected, under 35 U.S.C. § 103(a), as allegedly obvious over Mesnage in view of Loomis.

As discussed above, Mesanage does not suggest each and every element of the claimed invention, using as an example claim 16, which reads "an isolated antibody that binds EA1 antigen and specifically binds spores or vegetative cells of *B. anthracis*, but not *B. thuringiensis*". The missing elements are not supplied by Loomis. Thus, the requirements for a rejection based on obviousness, under 35 U.S.C. § 103(a), have not been met by these references. For at least these reasons, applicant respectfully requests withdrawal of this ground for rejection.

Remarks Regarding Prior Restriction Requirement

Applicant respectfully notes again that the above rejections appear to have been made based on antibodies of the invention and not the invention of claims 16-20 and 44-49, namely diagnostic kits. In other words, the prior Restriction Requirement to kits is being ignored in favor of an analysis based solely on antibodies. Thus, Applicant respectfully requests that the Restriction Requirement previously imposed on applicant be withdrawn and that all claims be examined in this application. Alternatively, the Examiner's 35 U.S.C. § 102/103 rejections above should be rendered moot as none of the cited references disclose kits.

Conclusion

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no.544612000100. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: August 16, 2004

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